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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,870	06/12/2006	Sergio Melotto	PB60212-1USW	2245

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EXAMINER	
RAMACHANDRAN, UMAMAHESWARI	
ART UNIT	PAPER NUMBER
1617	

NOTIFICATION DATE	DELIVERY MODE
04/16/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/552,870	MELOTTO, SERGIO	
	Examiner	Art Unit	
	UMAMAHESWARI RAMACHANDRAN	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/12/2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/12/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-18 are cancelled. Claims 19-35 are pending and are being examined on the merits herein.

Application Priority

This application is a 371 of PCT/EP04/042124, 4/16/2004 and claims priority of foreign application UK 0308968, 4/17/2003.

Information Disclosure Statement

The information disclosure statement (IDS) filed on 10/12/2005 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the IDS is being considered by the Examiner.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 19-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carlson et al. (US 6,117,855) in view of Armour et al. (U.S. 5,843,966).

Carlson teaches a product comprising a NK-1 receptor antagonist and an antidepressant or anti-anxiety agent as a combined preparation for simultaneous, separate or sequential use in the treatment or prevention of depression or anxiety (col. 50, claim 14). The reference teaches in col. 5, lines 61-62, paroxetine (SSRI) as one of the antidepressants (col. 43, claim 1, col. 50, claim 11) and teach a suitable dosage level for the antidepressant agent is about 0.5 to 1500 mg per day (col. 35, lines 48-50). The reference teaches in Example 2 a composition comprising an SSRI agent (20. 0 mg) and a NK-1 (50.0 mg).

The reference does not teach the compound [2-methoxy-5-(5-trifluoromethyl-tetrazol-1-yl)-benzyl]-([2S,3S]-2-phenyl-piperidin-3-yl)-amine] in a method of treating depression or anxiety.

Armour et al. teaches a pharmaceutical composition comprising [2-methoxy-5-(5-trifluoromethyl-tetrazol-1-yl)-benzyl]-([2S,3S]-2-phenyl-piperidin-3-yl)-amine] (example 7) and teach the compounds as NK1 antagonist. The reference also teaches a method for the treatment in a mammal of a condition mediated by tachykinins, comprising administration to said mammal of an effective amount of a pharmaceutical composition of a compound that includes 2-methoxy-5-(5-trifluoromethyl-tetrazol-1-yl)-benzyl]-([2S,3S]-2-phenyl-piperidin-3-yl)-amine] (col. 54, claim 14). The reference teaches that the compounds may also be useful in the treatment of CNS disorders in particular psychoses such as anxiety, depression etc. (col. 7, lines 3-7). The reference teaches a

proposed dose of the compound is 0.05 mg/kg to about 400 mg/kg bodyweight per day and it will be appreciated that it may be necessary to make routine variations to the dosage, depending on the age and condition of the patient and the precise dosage will be ultimately at the discretion of the attendant physician or veterinarian and the dosage will also depend on the route of administration and the particular compound selected.

It would have been obvious to one having ordinary skill in the art at the time of the invention to formulate a pharmaceutical composition comprising a dose of each paroxetine and [2-methoxy-5-(5-trifluoromethyl-tetrazol-1-yl)-benzyl]-([2S,3S]-2-phenyl-piperidin-3-yl)-amine] (hereinafter, piperidine compound A) compound and use the formulation in a method of treating depression or anxiety because of the prior art teachings of Carlson and Armour et al. Carlson teaches formulations comprising an SSRI agent such as fluoxetine and paroxetine and a NK-1 agent in a method of treating depression and anxiety. Armour et al. teaches the compound [2-methoxy-5-(5-trifluoromethyl-tetrazol-1-yl)-benzyl]-([2S,3S]-2-phenyl-piperidin-3-yl)-amine] as NK-1 antagonist and may be useful for CNS disorders such anxiety, depression etc. One having ordinary skill in the art would have been motivated to formulate such a composition and use the same in treating depression or anxiety in expectation of success because a composition comprising a NK-1 antagonist and an SSRI has been shown to be useful in a method of treating depression or anxiety. One of ordinary skill in the art would have been motivated to incorporate the two agents, paroxetine and [2-methoxy-5-(5-trifluoromethyl-tetrazol-1-yl)-benzyl]-([2S,3S]-2-phenyl-piperidin-3-yl)-amine] herein in a single combination pharmaceutical composition because combining

the agents herein known to be useful to treat depression individually into a single composition useful for the very same purpose is *prima facie* obvious. See *In re Kerkhoven* 205 USPQ 1069. The reference does not explicitly teach the amounts of paroxetine or piperidine compound A as claimed in the instant application. The dosage amount is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal amount of dosage in a method of treatment in order to best achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, this optimization of ingredient amount would have been obvious at the time of applicant's invention. The reference does not explicitly teach that the dose of each component is lower than normally expected to produce an effective therapeutic response in the treatment of depression or anxiety. It would have been obvious to one having ordinary skill in the art to adjust the dosage amounts to achieve desired therapeutic benefits. Also, it would have been obvious to one having ordinary skill in the art to lower the dosage amounts of the components paroxetine and piperidine compound A in the formulation in expectation of synergistic benefits as the reference Armour et al. teaches the compound piperidine compound A as NK1 antagonist and may be useful for treating depression and SSRI compounds are antidepressants and it known in the art the combination of NK-1 antagonist and paroxetine (SSRI) are known to be useful in treating depression (see Carlson).

Claims 33-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hefti (U.S. 6,162,805).

Hefti et al. teaches [2-methoxy-5-(5-trifluoromethyl-tetrazol-1-yl)-benzyl]-([2S,3S]-2-phenyl-piperidin-3-yl)-amine] or a pharmaceutically acceptable salt thereof as NK-1 receptor antagonists (col. 30, lines 40-45). The reference further teaches in claims 1, 4 (col. 41 and 42) a method of treating obesity comprising administering a NK-1 antagonist with an SSRI (selective serotonin reuptake inhibitor) compound such as paroxetine, fluoxetine etc such that together they give effective relief. The reference teaches such combinations may for example provide an enhanced anti-obesity effect. The reference also teaches that NK-1 receptor antagonist and the SSRI may be formulated in a single pharmaceutical composition or alternatively in individual pharmaceutical compositions for simultaneous, separate or sequential use (col. 34, lines 32-36). The reference further teaches that a suitable dosage level for the NK-1 receptor antagonist about 0.05 to 1500 mg per day and a suitable dosage level for the SSRI is about 0.5 to 1500 mg per day, preferably about 2.5 to 1000 mg per day, and especially about 2.5 to 500 mg per day (col. 36, lines 26-39). The reference teaches in Example 1 a composition comprising an SSRI agent (20. 0 mg) and a NK-1 (50.0 mg). It is taught in col. 1, lines 27-33 that neurokinin 1 (NK-1; substance P) receptor antagonists are being developed for the treatment of a number of physiological disorders associated with an excess or imbalance of tachykinins, and in particular substance P and examples of such conditions include disorders of the central nervous system such as anxiety, depression and psychosis (col. 1, lines 27-32).

It would have been obvious to one having ordinary skill in the art at the time of the invention to formulate a pharmaceutical composition comprising a dose of each paroxetine and [2-methoxy-5-(5-trifluoromethyl-tetrazol-1-yl)-benzyl]-([2S,3S]-2-phenyl-piperidin-3-yl)-amine] (hereinafter, piperidine compound A) compound because Hefti teaches formulations comprising an SSRI agent and a NK-1 agent. One having ordinary skill in the art would have been motivated to formulate such a composition because a composition comprising a NK-1 antagonist and an SSRI has been shown to be useful in a method of treating obesity. One of ordinary skill in the art would have been motivated to incorporate the two agents, paroxetine and [2-methoxy-5-(5-trifluoromethyl-tetrazol-1-yl)-benzyl]-([2S,3S]-2-phenyl-piperidin-3-yl)-amine] herein in a single combination pharmaceutical composition because combining the agents herein each of which is known to be useful to treat obesity individually into a single composition useful for the very same purpose is *prima facie* obvious. See *In re Kerkhoven* 205 USPQ 1069. The reference does not explicitly teach the amounts of paroxetine or piperidine compound A as claimed in claim 35 of the instant application. The amount of an ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal amount of ingredient to add in order to best achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, this optimization of ingredient amount would have been obvious at the time of applicant's invention. The reference does not

explicitly teach that the dose of each component is lower than normally expected to produce an effective therapeutic response in the treatment of depression or anxiety. As stated above, dosage is a parameter that can be routinely optimized and the recitation of the intended use, e.g. treatment of depression or anxiety does not lend patentable weight to composition claims. It would have been obvious to one having ordinary skill in the art to adjust the dosage amounts to achieve desired therapeutic benefits. Also, it would have been obvious to one having ordinary skill in the art to lower the dosage amounts of the components paroxetine and piperidine compound A in the formulation in expectation of synergistic benefits as the reference Hefti teaches NK1 antagonist and SSRI compounds are useful in treating obesity.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to UMAMAHESWARI RAMACHANDRAN whose telephone number is (571)272-9926. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SREENI PADMANABHAN/
Supervisory Patent Examiner, Art Unit 1617